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EXAMINER

WALICKA, MALGORZATA A

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--|---------------------------------------|--|
| Office Action Summary | Application No. 10/549,782 | Applicant(s) EGOROVA ET AL. | |
| | Examiner MALGORZATA A. WALICKA | Art Unit 1652 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 and 18-25 is/are pending in the application.
- 4a) Of the above claim(s) 2, 10 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-9, 11-13, 18-21 and 23-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on 19 September 2005 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Response to restriction requirement mailed March 3, 2008 is acknowledged. Claims 1-13 and 18-25 are pending. Claims 1, 3-9, 11-12, 13, 18-21, and 23-25 belonging to the elected group I are under examination. Claims 2, 10 and 22 are withdrawn from the examiner consideration as directed to a non-elected invention; see 37 CFR 1.142(b).

Detailed Action

Election/restriction

Applicant's election, with traverse, of Group I in the reply filed March 3, 2008 is acknowledged. The traversal is on the ground(s) that

- 1) Amidases of group I and II are derived from an enzyme isolated from *Pseudomonas thermophila*, and "are characteristic of enzymes for the same class";
- 2) group I and III should be rejoined, "See, e.g., MPEP 1850 ('The method for g unity of invention under PCT Rule 13 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories ').

Regarding item 1) Applicants seem to neglect the fact that amidase comprising SEQ ID NO: 2 is not a contribution over art as indicated during the prosecution of the PCT application of which the instant application is the national stage. The examiner in her restriction requirement used lack of contribution over the art as the base for lack of unity between group I and II. Thus, the restriction between group I and II is proper.

Regarding item 2), MPEP 1850, page 1800-101, third paragraph, states that extensive combinations should be looked carefully to ensure that the requirements of both PCT Rule 13 (unity of invention) and PCT Article 6 (conciseness of claims) are satisfied. "While a single set of independent claims according to one of (A), (B), or (C) above is always permissible" it does not require the International Authority to accept a plurality of such sets. This is in accord with 37 CFR 1.475 quoted by the examiner in the restriction requirement. In the disputed case claim 22 is directed, in an alternative, to two different methods. One of the method is a repetition of the method of claim 18, and the other, "a

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method of acylation", is different, because it requires different activity of the same protein and has a different effect, i.e. results in synthesis of a different chemical product than that of the method of claim 18.

Restriction between Group I and claim 22 is, therefore, proper.

In result of change of the dependence of claims 23 made in response to the restriction requirement, claims 23-25 belong now to Group I. Claim 22 consists group III. The restriction is, for all the reasons discussed above, and presented in the restriction requirement of Jan. 3, 2008, proper and MADE FINAL.

Claims 1, 3-9, 11-13, 18-21 and 23-25 belonging to Group I are under examination.

Priority

Acknowledgment is made of Applicant's claim to the benefits of the German application 10312842.5 filed March 21, 2003.

Objections

1. Descriptions of Figures 1-7. do not state to which enzyme(s) disclosed by applicants_and summarized in Table 4 the figures refer to. Do they refer to the enzyme of SEQ ID NO: 3? Figures 3 and 4 are objected as missing description of y-axis.
2. Table 3 is objected to because it does not identify the enzyme having specificity listed in the Table. Particularly it is not clear whether the Table refers to the properties of amidase of SEQ ID NO: 3 fully identified in the disclosure by its structure.
3. The specification is objected to because the specification is not clear as to whether all of the amidases isolated by applicants indeed comprise SEQ ID NO:1 or a sequence being at least 50% identical to SEQ ID NO: 1.
4. Table 4 appears as the first in the text of the specification. Tables 1, 2 and 3 are after Table 4. Please renumber the Tables.

Rejections

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35 USC section 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-9, 11-13, 18-21 and 18-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The base claim 1, is reciting a multimeric amidase. The specification does not define the term "multimeric". The claim however is not clear about how many subunits are involved in the structure of the claimed amidase; two, fifteen? Table 4 lists amidases that comprise from 1 to 8 units. The claims, however, are not limited to reflect that fact.

35 USC section 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written description

Claim 1, 3-9, 11-13, 18-21 and 18-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The base claim 1 is rejected as lacking sufficient written description of the structure of the claimed amidase. The claim is directed to

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- 1) any amidase containing SEQ ID NO: 1, a nine amino acid long peptide, or a peptide being at least 50% homologous to SEQ ID NO: 1, wherein
- 2) the peptidase may be a monomeric or multimeric protein.

The claim is generic and lacks sufficient description of structure of the product it is directed to. Amidases are proteins containing several hundreds of amino acids, for example, the amidase of SEQ ID NO: 3 having a fully disclosed structure is 509 amino acid long. The polypeptide of SEQ ID NO: 1 consists of less than 2% of SEQ ID: 3. Thus, SEQ ID NO: 1 does not provide for the structure of the full length enzymatically active protein, or even for a catalytically active fragment of SEQ ID NO: 3, not to speak about other amidases, even amidases disclosed in Table 4. In addition, the disclosure does not teaches any particular function of SEQ ID NO: 1 and 2. Thus it is unknown what function is to be preserved in the at least 50% homologs thereof.

In addition, the scope of the claim encompasses amidases that are monomers or multimers, but the claim does not recite how many units are in these proteins. It is also not known if the units are the same or different. Altogether, the structure of the claimed protein is not sufficiently described.

Furthermore, claim 1 is lacking sufficient description of function, because amidases, as a skilled artisan realizes, are specific for different substrates. Table 3 provides data on activity of the isolated amidases, but it is actually not written to which amidase(s) the data of Table 3 refer to.

Claim 3 is also rejected, because the further limitation to contain SEQ ID NO: 2 does not provide for the structure of the claimed polypeptide. The 23 amino acids (9+14) are only a few percent of an amidase structure; for example, 4.5 % of SEQ ID NO: 3. Other rejected claims provide additional limitation on the scope of claim 1, however only claim 12 provides in alternative, the fully identifying characteristics of the claimed enzyme.

The methods of claims 18-25 are generic for amides that are substrates of the product of claim 1. Therefore, the claims are lacking written description of the substrates that are hydrolyzed by the amidase of claim 1. The scope of claim 18 is particularly broad, because it covers any amide. The scope of claim 23 narrows all amides to their different groups, but even that is too broad and has no support in the

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disclosure. Disclosure, which in Table 3 lists hydrolyzing activities of the amidase of invention, is lacking written description of which amidases presented in Table 4 are having substrates of Table 3.

In conclusion, applicants have failed to sufficiently describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention at the time the application was filed.

3.2.2. Scope of enablement

Claims 1, 3-9, 11-13, 18-21 and 18-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the amidase of SEQ ID NO: 3, a thermostable amidase from *Pseudonocardia thermophila*, encoded by DNA molecule of SEQ ID NO: 4, does not reasonably provide enablement for the broadly claimed amidases and methods of their use.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breadth of the claims covers any amidase containing SEQ ID NO: 1 or a sequence having a homology greater than 50% with SEQ ID NO: 1 wherein the amidase may, in addition, comprise SEQ ID NO: 2 or a peptide having at least 50% homology to SEQ ID NO: 2.

While isolation of proteins and determining their enzymatic activity is relatively well developed, the broad scope of the claims directed to an extremely large and versatile genus of amidases imposes on the skilled artisan experimentation that is not routine. It requires isolating a protein, determining whether it has any amidase activity, sequencing its N-terminus, and in case of claim 2, finding whether protein comprises SEQ ID NO: 2 or its homolog being at least 50% identical to SEQ ID NO: 2.

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Regarding the function of the claimed protein, claims 1 and 3 do not define an actual specific reaction in which the claimed amidase participates and although the specification describes many substrates, and amidase activities, one having skills in the art would not know which of them to select for determining whether the newly isolated enzyme has the required activity of amidase, this imposes not a routine experimentation.

Regarding the structure, the presence of SEQ ID NO:1 or even SEQ ID NO: 1 and 2 in the claimed protein, does not provide a sufficient guidance as to the rest of the amino acid sequence of the claimed amidase that determines its function; see the above rejection for lack of written description. The disclosure does not provide any guidance as to what role, if any, both sequences possess in the activity of the claimed enzyme. For that reason, the disclosure fails to teach which modification of SEQ ID NO: 1 and 2 lead to their at least 50% homolog having the same role in the structure of the claimed enzymes.

Claims 12 and 13 are rejected because the disclosure does not provide any guidance on how to modify SEQ ID NO: 3 /its encoding SEQ ID NO: 4, so that the claimed protein had at least 50% homology and the same function and the encoding sequence 60% homologous to SEQ ID NO: 4. Both claims require from a skilled artisan testing astronomical numbers of variants of SEQ ID NO: 3/4. Applicants' attention is turned to the fact that the total number of muteins having 50% identity, not homology, of the protein of 509 amino acids is $[509! \times 19^{254}] / [(509 - 254)! \times 254!]$. Testing this number of muteins is certainly out the routine.

Altogether providing amidase of SEQ ID NO: 3 having SEQ ID NO: 1 in positions 2-10 and SEQ ID NO: 2 in positions 471- 484 is not a sufficient guidance as to the structure of other broadly claimed enzymes. As to the specificity of the claimed protein, while the enablement is not precluded by a routine experimentation, when the experimentation is not routine, should provide a reasonable amount of guidance as to the activity and structure of the claimed enzyme. Otherwise, the experimentation imposed on the skilled artisan has a low probability of success and is undue.

Conclusion

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Claims 1, 3-9, 11-13, 18-21 and 18-25 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed, can be reached on (571) 272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.

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Patent Examiner

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